REMARKS

Formal Matters

Applicants note that the rejections under 35 U.S.C. § 112, second paragraph have not been maintained in the present Office Action and are therefore deemed withdrawn.

Claims 1-22 are pending in this application.

Information Disclosure Statement

The Office stated that it failed to receive a copy of the 31 documents cited in the Information Disclosure Statement filed April 3, 2002. (Office Action at ¶ 3.) Applicants provide an additional copy of the 31 references and the Form 1449, which were previously submitted on April 3, 2002, as reflected in the attached postcard receipt. Applicants respectfully request that the Examiner indicate that these references have been considered on the resubmitted Form 1449.

Rejection under 35 U.S.C. § 102

The Office rejected claims 1-4 and 7-9 under 35 U.S.C. § 102(b) as being anticipated by *Palomäki* (Journal of Immunological Methods, Vol. 145, (1991) pages 55-63). (Office Action at ¶ 5.) The Office stated that *Palomäki* teaches

> a enzyme immunoassay (EIA) for the detection of hepatitis B surface antigen (HBsAg) in human serum or plasma using a monoclonal antibody Mab1 coated to a solid phase (R1 + solid phase) and incubated with HbsAg and a peroxidase labeled polyclonal antibody (HRP-Pab), which the examiner considers to be (R2 + L1) and a second peroxidase labeled monoclonal antibody Mab2 (HRP-Mab2), which the examiner considers to be (R3 +L2) to form sandwich complexes.

(Office Action at ¶ 5.) For the reasons discussed below, Applicants traverse this rejection and respectfully disagree with the Office's assertions regarding the teachings of *Palomäki*.

Applicants' claim 1 reads as follows:

> 1. A method for detecting an analyte A in a sample, comprising:
>
> incubating an incubation mixture comprising a sample with an analyte A-specific binding partner R1, which is associated with a solid phase, an analyte A-specific binding partner R2, which is associated with a label L1, and an analyte A-specific binding partner R3, which is associated with a label L2, wherein saturation of analyte A-binding sites of the binding partner R2 takes place at a) a higher analyte A concentration, b) at a later time in the incubation, or c) at a higher analyte A concentration and at a later time in the incubation, than does saturation of analyte A-binding sites of the binding partner R3; and
>
> determining an L1-dependent measurement signal at a different time from an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal, or determining the L1-dependent measurement signal using a different measurement method than used to determine the L2-dependent measurement signal or the L1 plus L2-dependent measurement signal.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. § 2131. Contrary to the Office's assertion, *Palomäki* fails to teach the measurement limitations recited in independent claim 1. Specifically, *Palomäki* fails to teach "determining an L1-dependent measurement signal at a <u>different time</u> from an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal, or determining the L1-dependent measurement signal using a <u>different measurement</u>

method than used to determine the L2-dependent measurement signal or the L1 plus L2-dependent measurement signal." (emphasis added.) The Office stated that "[a]bsorbances at 450 nm were measured using a microtitre plate reader, which the examiner interprets to be L1 and L2 measurements." (Office Action at ¶ 5 (citations omitted).) Applicants respectfully note, however, that the entity HRP-Mab2 is contacted with the fluid at the same time that the other entities HRP-Pab and Mab1 are contacted with the fluid, and not after the measurement of HRP-Pab. (*Palomäki,* page 57, right column, fifth paragraph.) *Palomäki* teaches that a single absorbance measurement is taken after the conjugate incubation and washing steps. *Id*. Applicants, on the other hand, claim the taking of at least two measurements at different times or with different measurement methods.

In addition, the Office asserts that "a separate measurement was taken at optimal concentration when the HRP-Pab-HbsAg was used alone or simultaneous with diluted HRP-Mab2-HbsAg in the assay." (Office Action at ¶ 5.) The measurements taken in these two different assays also do not constitute "determining an L1-dependent measurement signal at a different time from an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal, or determining the L1-dependent measurement signal using a different measurement method than used to determine the L2-dependent measurement signal or the L1 plus L2-dependent measurement signal," as independent claim 1 recites. *Palomäki* teaches the use of HRP-Pab-HbsAg alone merely as a method to optimize its concentration for use together with HRP-Mab2-HbsAg in a separate assay. The assay employing HRP-Pab-HbsAg alone

demonstrates that use together with HRP-Mab2-HbsAg reduces the hook effect and increases sensitivity. (*See, e.g.*, *Palomäki*, Figures 2 and 4.) *Palomäki* does not teach adding an additional antibody after taking an absorbance measurement with the HRP-Pab-HbsAg label alone in the mixture. Rather, "[t]est samples and controls (50µl) were added to the microtitre wells simultaneously with the HRP-Pab and HRP-Mab2 conjugates." (*Palomäki*, page 57, right column, fifth paragraph (emphasis added).) Only after incubation and washing was the single absorbance measurement taken.

Claim 1 requires that the incubation mixture comprise "a sample with an analyte A-specific binding partner R1, which is associated with a solid phase, an analyte A-specific binding partner R2, which is associated with a label L1, and an analyte A-specific binding partner R3, which is associated with a label L2." (*See also* Specification, pages 36-37, examples 11 and 12.) An absorbance measurement when HRP-Pab-HbsAg is used alone does not fulfill these requirements. Furthermore, an absorbance measurement when HRP-Pab-HbsAg and HRP-Pab-HbsAg are used together, but only one absorbance measurement is taken, does not fulfill the measurement limitations of claim 1, as discussed above. For at least the reasons discussed above, the *Palomäki* reference does not teach all the elements of claim 1. Therefore, Applicants respectfully contend that *Palomäki* does not anticipate claims 1-4 and 7-9 and ask that this rejection be withdrawn.

Rejections under 35 U.S.C. § 103

The Office rejected dependent claims 5 and 6, independent claim 19, and its dependent claims 20-22 under 35 U.S.C. § 103 as being unpatentable over *Palomäki* in

view of *Marquardt* (U.S. Patent No. 6,610,494). (*See* Office Action at ¶ 7.) Applicants respectfully traverse.

In order to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) all claim limitations must be taught or suggested, (2) there must be some suggestion or motivation to modify the references or combine reference teachings, and (3) there must be a reasonable expectation of success. M.P.E.P. § 2143.03.

Applicants respectfully submit that the references provided by the Office do not teach or suggest all claim limitations.

Due to the dependency of claims 5-6, the limitations of claim 1 must be read into claims 5-6 when determining the alleged obviousness of claims 5-6. For the reasons discussed above, *Palomäki* does not expressly teach the measurement claim limitations of "determining an L1-dependent measurement signal at a different time from an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal, or determining the L1-dependent measurement signal using a different measurement method than used to determine the L2-dependent measurement signal or the L1 plus L2-dependent measurement signal," as independent claim 1 recites. *Palomäki* teaches a single absorption measurement of the incubation mixture. Furthermore, *Palomäki* does not suggest more than one measurement signal at different times. *Marquardt*, which teaches a method of detecting via a solid-phase assay the amount of biological activity and/or the quantity of a biologically active substance, does not cure the defects of *Palomäki*. In fact, none of the references cited by the Office teach or suggest the measurement limitations of the pending claims. Applicants therefore respectfully submit

that all of the limitations of claims 5 and 6 are not taught or suggested by the cited references. Therefore, the Office has not established a *prima facie* case of obviousness and the rejection of claims 5 and 6 should be withdrawn.

For many of the same reasons discussed above, *Palomäki* and *Marquardt* do not teach or suggest all the claim limitations of independent claim 19 and dependent claims 20-22. For instance, *Palomäki* does not teach a binding partner R3 (*e.g.*, HRP-Mab2) associated with a member X of a specific binding pair, as claim 19 requires. (*See also* Specification, Figure 1.) Nor does *Palomäki* teach or suggest the measurement limitations of claim 19, which are identical to the measurement limitations of claim 1, as discussed above. *Marquardt* also fails to teach or suggest the measurement limitations of claim 19. Furthermore, *Marquardt's* alleged disclosure of an XY binding pair fails to teach or even suggest any of the other limitations as claimed in claim 19, such as "a sample with an analyte A-specific binding partner R1, which is associated with a solid phase, an analyte A-specific binding partner R2, which is associated with a label L1, and an analyte A-specific binding partner R3, which is associated with a label L2." Thus, *Palomäki* in view of *Marquardt* does not render Applicants' claim 19 obvious. Nor do these references make obvious the more narrow limitations of claims 20-22. Applicants respectfully request that this rejection be withdrawn.

The Office also rejected claims 10-15 under 35 U.S.C. § 103 as being unpatentable over *Palomäki* in view of *Cragle* (U.S. Patent No. 4,590,169). (Office Action at ¶ 8.) Specifically, the Office stated that *Cragle* teaches "that binding entities use particles for direct particle agglutination assays, wherein the particles become

aggregated if the antigen is in the sample and this protocol can be performed in one step." (Office Action at ¶ 8.)

Applicants traverse this rejection. *Palomäki* and *Cragle* do not teach or suggest all the limitations of claims 10-15. Due to the dependency of claims 10-15, the limitations of claim 1 must be read into claims 10-15 when determining the alleged obviousness of claims 10-15. For the reasons discussed above, the *Palomäki* does not teach or suggest the measurement claim limitations of "determining an L1-dependent measurement signal at a different time from an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal, or determining the L1-dependent measurement signal using a different measurement method than used to determine the L2-dependent measurement signal or the L1 plus L2-dependent measurement signal," as independent claim 1 recites.

These deficiencies of *Palomäki* that fail to teach or make obvious Applicants' invention cannot be found within the four corners of *Cragle*. The *Cragle* patent is directed to a direct particle agglutination assay for an antigenic substance which comprises contacting a fluid with an antibody (Ab) coated particle (P). The fluid is also contacted with a second antibody (Ab_a) coated particle (P_1). *Cragle*, however, does not teach or even suggest "determining an L1-dependent measurement signal at a different time from an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal, or determining the L1-dependent measurement signal using a different measurement method than used to determine the L2-dependent measurement signal or the L1 plus L2-dependent measurement signal," as independent claim 1

recites. *Palomäki* and *Cragle*, as demonstrated above, fail to teach or suggest all the limitations of Applicants' claims 10-15. Therefore, Applicants respectfully request that this obviousness rejection be withdrawn.

The Office also rejected claims 16 and 17 under 35 U.S.C. § 103 as being unpatentable over *Palomäki* in view of *Pitner* (U.S. Patent No. 5,641,629). Specifically, the Office stated that *Pitner* teaches "that energy transfer techniques offers a sensitive and simple method of measuring the binding of specific analytes or target molecules." (Office Action at ¶ 9.)

Applicants traverse this rejection. *Palomäki* and *Pitner* do not teach or suggest all the limitations of claims 16 and 17. Due to the dependency of claims 16 and 17, the limitations of claim 1 must be read into claims 16 and 17 when determining the alleged obviousness of claims 16 and 17. For reasons discussed above, *Palomäki* does not teach or even suggest Applicants' claim limitations of "determining an L1-dependent measurement signal at a different time from an L2-dependent measurement signal or an L1 plus L2-dependent measurement signal, or determining the L1-dependent measurement signal using a different measurement method than used to determine the L2-dependent measurement signal or the L1 plus L2-dependent measurement signal."

These deficiencies of *Palomäki* that fail to teach or make obvious Applicants' invention cannot be found within the four corners of *Pitner*. *Pitner* is directed to using spectroscopically detectable labeled molecules to determine the presence of a target compound in a sample. (*See*, e.g., Abstract.) *Pitner*, however, does not teach or even suggest "determining an L1-dependent measurement signal at a different time from an

L2-dependent measurement signal or an L1 plus L2-dependent measurement signal, or determining the L1-dependent measurement signal using a different measurement method than used to determine the L2-dependent measurement signal or the L1 plus L2-dependent measurement signal," as claim 1 requires. *Palomäki* and *Pitner*, as demonstrated above, fail to teach or suggest all the limitations of Applicants' claims 16 and 17. Therefore, Applicants respectfully request that this obviousness rejection be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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